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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/705,985	11/03/2000	Dirk M. Anderson	2874-B	6890

37582 7590 02/08/2005

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EXAMINER	
STANDLEY, STEVEN H	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/705,985	ANDERSON ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *03 November 2000*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,9,11,13,15,16,18,20,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,9,11,13,15,16,18,20,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Withdrawn Rejections

1. Applicant has amended claims 5 and 13 in response to the examiner's rejection under 35 U.S.C. 112, 2nd paragraph holding that the phrase "ameliorating the effects of excess bone loss" is indefinite. Claims 5 and 13 now read, "inhibiting RANKL-induced osteoclastogenesis in a patient in need thereof." Furthermore, claim 5 and 13 has been amended in response to examiner's rejection to eliminate reference to patients whom are "at risk from" one of the listed conditions. Part (c) of claim 5 and 13 was amended by applicant to refer to a RANK polypeptide comprising amino acids 33-213 instead of a polypeptide comprising amino acids 1-213 of SEQ ID NO: 2. By doing so, applicant states that claims 11 and 15, which were held not to be further limiting from the claims on which they depended, are now narrower than their base claim. Claims 9, 16, 18, 20, 25 and 26 depend on claims that were held indefinite and were therefore rejected under 35 U.S.C. 112 2nd paragraph as well. The examiner finds applicant's changes with respect to the rejection under 35 U.S.C. 112 2nd paragraph persuasive. Therefor the rejection under 35 U.S.C. 112 2nd of claims 5, 9, 11, 13, 15, 16, 18, 20, 25, and 26 is withdrawn.

Applicant has asserted in the paper dated November 3, 2000, that "increased numbers of osteoclasts and increased osteoclastic bone resorption are observed in patients suffering from several types of cancer that are recited in claims 5 and 13 [page 4, bottom]," in response to the examiner's rejection of claims 5, 9, 11, 13, 15, 16, 18, 20, 25, and 26 under 35 U.S.C. 112 1st paragraph for lack of enablement. Applicant further

cites 2 reviews on pages 2 and 7 of the specification. The examiner has found each cancer claimed in claims 5 and 13 to be disclosed as associated with hypercalcemia, which in turn can be caused by the increased presence of osteoclasts due to "humoral...and local factors secreted by the tumor [Guise and Mundy, cited on page 7 line 21 of the specification]." Furthermore, Guise and Mundy explain that, while there are subcategories of hypercalcemia produced by malignancies, "the mediators may be identical except that in one situation it is a local mediator while in another it is a humoral mediator." Given the statements by Guise and Mundy, the examiner finds that one skilled in the art would have a reasonable expectation that using soluble RANK peptide to inhibit RANKL-induced osteoclastogenesis would work in the types of cancer recited by the applicant. Therefor, the rejection claims 5, 9, 11, 13, 15, 16, 18, 20, 25, and 26 under 35 U.S.C. 112 1st paragraph for lack of enablement is withdrawn.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5, 9, 11, 18, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al (filed 12/22/97; US Patent # 6,017,729), and further in view of Fisher et al (1995).

Claims 5 is an independent claim to "a method of inhibiting RANKL-induced osteoclastogenesis in a patent in need thereof, comprising administering to said patient a soluble RANK polypeptide composition, wherein said patient suffers from a condition selected from the group consisting of ...Breast cancer, and further wherein the soluble RANK polypeptide is capable of binding a RANKL polypeptide that consist of amino acids 1-317 of SEQ ID: 8 and selected from the group consisting of: (a) a polypeptide encoded by a DNA that encodes a protein comprising amino acids 33-196 of SEQ ID NO: 2, (b) a polypeptide encoded by an DNA that is capable of hybridizing to a DNA consisting of the nucleotide sequence shown in SEQ ID NO:1 under stringent conditions, wherein stringent conditions comprise hybridizing at 63°C in 6X SSC; (c) a polypeptide that is at least 80% identical in amino acid sequence to a RANK polypeptide comprising amino acids 33-213 of SEQ ID NO:2 and (d) a polypeptide comprising amino acids 33-213 of SEQ ID NO:2, and further wherein said composition is administered in amounts sufficient to inhibit RANK-induced osteoclastogenesis.

Anderson et al. teach a RANK polypeptide (Anderson et al., SEQ ID NO: 5; SEQ ID NO: 1 in the instant specification) capable of binding to RANKL polypeptide (Anderson et al., SEQ ID NO: 13) that consists of amino acids 1-317 (designated SEQ ID NO: 8 in the instant specification). Anderson et al. also disclose a polypeptide encoded by a DNA that encodes a protein comprising amino acid sequence 1-213 or a fragment thereof, of SEQ ID NO: 2 of the instant application (designated SEQ ID NO: 6 in Anderson et al; for example in column 4, lines 42-58). This teaching meets the limitation of "a polypeptide" recited in part (a) of claim 5. Furthermore, Anderson et al. disclose the soluble peptide as being "useful as an adjunct therapy [to radiation treatment] for diseases characterized by neoplastic cells [Anderson et al, column 16, lines 24-28]."

Claim 9 is dependent upon claims 5, and further limits by claiming RANK in the method of treatment that further comprises an immunoglobin Fc and an immunoglobin Fc mutein, a FLAG tag, a peptide comprising at least 6 His residues, a leucine zipper, and combinations thereof. Anderson et al. disclose a RANK polypeptide fused with an FC domain (See Anderson et al., Figure 1 and column 5, lines 25-27).

Claim 11 is directed at the base claim method of claim 5, and is the method wherein the soluble RANK is at least 80% identical to amino acids 33-213 of SEQ ID NO2. Anderson et al. state that "[any] fragments of the extracellular domain will also provide soluble forms of RANK [column 4 lines 48-50]," and further contemplate that "In a preferred embodiment, RANK polypeptides are at least about 80% identical in amino acid sequence to the native form of RANK [column 9, lines 20-26]."

Claims 18 and 25 are dependent on the base claim 5. Claim 18 is to a RANK polypeptide with an Fc domain (SEQ ID NO 3) or a Leucine zipper domain (SEQ ID 6). Anderson et al disclose both a RANK-Fc and a RANK-Leucine zipper fusion protein (see Anderson et al., Example 15; Anderson et al., column 5 lines 45-48). Both functional elements are present and the inventions of Anderson et al. have the same properties. Claim 25 is to a soluble RANK polypeptide of SEQ ID 2 and an Fc fusion of SEQ ID NO 3. As indicated above, Anderson et al state that "[any] fragments of RANK extracellular domain will also provide soluble forms of RANK." Furthermore Anderson et al. disclose a fusion of RANK polypeptide with an FC domain (as indicated above).

Anderson et al. do not teach radiation therapy as a treatment for breast cancer.

Fisher et al (1995) teach that "after 12 years of follow-up, findings continue to indicate that lumpectomy ***followed by breast irradiation*** is appropriate therapy for women with stage I or II breast cancer [page 1461, last paragraph]." Therefore, because Anderson et al. disclose the invention for use as an adjunct to radiation treatment and Fisher et al teach that radiation therapy is appropriate for breast cancer, it would have been obvious to one skilled in the art at the time to use soluble RANK as an adjunct to radiation treatment of breast cancer. The motivation is provided by Anderson et al. who state that "tumor cells are more responsive to radiation when their NF-Kappa B is blocked [by soluble RANK; column 16 line 24].

Claims 13, 15, 16, 20, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al (filed 12/22/97; US Patent # 6,017,729), and further in view of Mayer et al (1997).

Claim 13 is directed to a method of RANKL-induced osteoclastogenesis as described above for claim 5 with the exception of which patient population it is directed to. Claim 13 is a method of inhibiting..."wherein said patient suffers from a condition selected from the group consisting of squamous cell carcinoma, lung cancer, prostate cancer..." Moreover dependent claims 15, 16, 20, and 26 recite the same limitations to claim 13 that claims 9,11, 18, and 25 recite to claim 5. Therefore, with respect to claims 13, 15, 16, 20, and 26, Anderson et al. teach as described above for claims 5, 9, 11, 18, and 25.

Anderson et al. do not teach radiation therapy as a treatment for lung cancer.

Mayer et al. teach radiation therapy in lung cancer, indicating that "After surgery, external-beam ***radiation is the most effective single treatment modality*** in the treatment of non-small cell lung cancer [page 954, first paragraph]." Therefore, because Anderson et al. disclose the invention for use as an adjunct to radiation treatment and Mayer et al teach that radiation therapy is appropriate for lung cancer, it would have been obvious to one skilled in the art at the time to use soluble RANK as an adjunct to radiation treatment of breast cancer. The motivation is provided by Anderson et al. who state that "tumor cells are more responsive to radiation when their NF-Kappa B is blocked [by soluble RANK; column 16 line 24].

Summary

3. Any inquiry concerning this communication should be directed toward examiner Steven Standley (Ph: 571-272-3432). The examiner can normally be reached Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the Steven Standley fail, the examiners' supervisor, Anthony Caputa, can be reached at (571 272-0829).

Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (toll free) 866-217-9197.

Steven H. Standley, Ph.D.

1/25/2005

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER